IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

Hospira, Inc. *
275 N. Field Drive
Lake Forest, IL 60045, *

Plaintiff, *

v. * CIVIL ACTION NO.

Sylvia Mathews Burwell, Secretary *
U.S. Department of Health and Human
Services *
200 Independence Ave., S.W.
Washington, D.C., 20201, and *

Dr. Margaret Hamburg, Commissioner *
U.S. Food and Drug
Administration *
10903 New Hampshire Avenue
Silver Spring, MD 20993 *

U.S. Food and Drug *
Administration
10903 New Hampshire Avenue *
Silver Spring, MD 20993
*
Defendants.
*

SERVE ON:

Sylvia Mathews Burwell, Secretary
U.S. Department of Health and Human
Services
200 Independence Ave., S.W.
Washington, D.C., 20201, and

Dr. Margaret Hamburg, Commissioner
U.S. Food and Drug
Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

* * * * * * *

COMPLAINT

Plaintiff Hospira, Inc. ("Hospira") brings this action for declaratory and injunctive relief against Defendants the Secretary of the U.S. Department of Health and Human Services, the Commissioner of the U.S. Food and Drug Administration ("FDA"), both in their respective official capacities, and against FDA. For its complaint, Hospira alleges as follows:

Preliminary Statement

1. Hospira is the owner of a prescription drug that it markets under the brand name PRECEDEX™ (hereinafter "Precedex"). Hospira brings this action and its accompanying motion for immediate and preliminary injunctive relief because the FDA has taken a final agency action which adversely affects and imminently threatens irreparable harm to Hospira. Hospira challenges (a) FDA's final decision in Docket No. FDA-2014-N-0087 issued on August 18, 2014 (the "FDA August 18 Decision" or "FDA Decision") (Ex. A); (b) FDA's final approval of one or more generic versions of Precedex based upon FDA's August 18 Decision; and (c) FDA's authority to grant any final approvals of generic version of Precedex based upon FDA's August 18 Decision. As detailed in this complaint, FDA's August 18 Decision is based on a clear error of law and is directly contrary to the decision of the Supreme Court in *Caraco Pharm. Labs. Ltd. v. Novo Nordisk A/S*, 132 S. Ct. 1670 (2012). Further, because FDA's August 18 Decision is a "rule" within the meaning of and subject to the rulemaking requirements of Administrative Procedure Act, 5 U.S.C. § 553, the Decision is unlawful because the "rule" was "adopted" without complying with the Act's mandatory rulemaking requirements.

2. FDA's Decision is an unlawful application of FDA's exceedingly limited authority under 21 U.S.C. § 355(j)(2)(A)(viii) to approve a generic version of a brand drug in the absence of the generic's certifying that it does not infringe the predicate brand drug's patent(s).

A generic applicant may seek approval under 21 U.S.C. § 355(j)(2)(A)(viii) only when (a) FDA has approved more than one use (indication) for the predicate brand drug, *and* (b) at least one of those indications is not covered by any of the brand's patents. *See id.*; 21 C.F.R. § 314.94(a)(12)(iii)(A); *see generally Caraco*, 132 S. Ct. at 1677. Under the limited 21 U.S.C. § 355(j)(2)(A)(viii) process and authority, the generic must propose a label that "carves-out" from the brand drug's approved labeling the patented method(s) of use. *See* 21 C.F.R. § 314.94(a)(8)(iv). The FDA's role is ministerial only and it may only approve such a carve-out where there is no overlap between the brand's description of the method of use protected by the patent (the "use code"), and the indications remaining in the generic's proposed labeling. As a matter of fact and as a matter of law, that narrow section viii exception is inapplicable here and FDA's attempt to invoke its limited § 355(j)(2)(A)(viii) authority in this instance is improper, unjustified, and contrary to law.

3. In this matter, FDA acted contrary to law and to the Supreme Court's decision in *Caraco* when the agency determined that it could approve a generic even where FDA acknowledges that there is overlap between Hospira's description of the method of use and the indications in the generic's labeling. Ex. A at 1. Assuming, without conceding that FDA could lawfully adopt the "rule" set forth in its August 18 Decision, FDA could so only by complying with the rulemaking requirements of the Administrative Procedure Act and those requirements were not followed here.

4. This Court's immediate intervention is necessary to prevent irreparable harm to Hospira. As a direct result of FDA's Decision, and notwithstanding the law to the contrary, the market will be flooded immediately with generic versions of Precedex, with resulting certain immediate irreparable damage to Hospira, its employees, its market position, its reputation, its

relationships with customers, and its business interests. Hospira asks the Court to temporarily, preliminarily, and permanently enjoin implementation of FDA's Decision, including ordering FDA to rescind ab initio any and all final decisions approving generic versions of Precedex, ordering FDA to recall any product sold or distributed under such an approval, and/or allowing the marketing of generic versions of Precedex predicated on the August 18 Decision, and enjoining FDA from issuing any further or additional final decisions approving generic versions of Precedex or allowing the marketing of generic versions of Precedex predicated on the August 18 Decision.

Parties

5. Plaintiff Hospira is in the business of manufacturing and selling prescription drugs and medical devices. It is based in Lake Forest, Illinois.

6. Defendant Sylvia Mathews Burwell is sued in her official capacity as the Secretary of the U.S. Department of Health and Human Services ("HHS"), a cabinet-level agency of the executive branch of the United States Government. Defendant FDA is a major operating division of HHS.

7. Defendant Dr. Margaret Hamburg is sued in her official capacity as the Commissioner of FDA, an agency of the United States Government within HHS. The Secretary of HHS has delegated to FDA and its Commissioner the authority to administer the relevant provisions of the federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301-399(a) *et seq.*, including decisions relating to the approval of new prescription drugs. Defendant FDA is the agency of the United States Government which administers the FDCA. The decision challenged in this case is a final agency action of FDA.

Jurisdiction and Venue

8. This action arises under federal law, specifically the FDCA and the Administrative Procedure Act ("APA"); therefore, this Court has subject matter jurisdiction pursuant to 28 U.S.C. § 1331. Pursuant to 28 U.S.C. §§ 2201-2202, the Court is authorized to grant Hospira's prayers for declaratory relief.

9. Venue is proper in the District of Maryland pursuant to 28 U.S.C. § 1391(e) because both defendants regularly conduct business in this district.

Statement of Facts

A. Background Regarding New Drug Review and Approval

10. FDA must approve a prescription drug before the drug may be sold or distributed in interstate commerce. For new drugs, sometimes called "innovator" or "brand" drugs, the FDCA requires submission to FDA of a new drug application ("NDA"). An NDA must include evidence of the drug's safety and effectiveness—typically demonstrated by an applicant's submission of data from comprehensive, multi-phase clinical trials that take years to complete—and the applicant's proposed labeling for the drug that specifies, among other things, indications for use, contra-indications, routes of administration, and safety information concerning side effects and adverse events associated with the drug's indicated uses.

11. The process of preparing and submitting an NDA involves an extraordinary investment of an NDA applicant's time and money, with no guarantee that the subject drug will ever be approved by the FDA or, if approved, that the drug will be successful in the marketplace. To justify this costly and risky investment, an NDA applicant relies on patent protection to ensure that, at least for some measurable period of time, it will have the exclusive right to market its drug for its approved indicated uses.

12. As part of the NDA process, the NDA holder must submit information about patents that cover the subject drug, including the patents' expiration dates and a use code description. *See* 21 C.F.R. § 314.53(c)(2)(ii)(P)(3), (e).

13. In 1984, the Hatch-Waxman Amendments to the FDCA were enacted, authorizing FDA to consider and approve abbreviated new drug applications ("ANDAs") for generic equivalents of innovator drugs whose safety and efficacy had already been demonstrated through the lengthy NDA process. Rather than investing the significant time and money that would be required to establish independently the safety and efficacy of a proposed generic drug, an ANDA applicant may rely on the safety and efficacy data contained in the NDA, but only if the generic has the same active ingredients and routes of administration, has the same labeling (including indications of use, *i.e.*, FDA approved uses for which the drug may be prescribed), and is "bioequivalent" to the innovator drug. *See* 21 U.S.C. § 355(j)(2)(A)(ii)-(v).

14. Entry of an ANDA into the market raises patent issues if the NDA holder claims patent protection for the drug substance (active ingredient), drug product (formulation or composition), or method(s) of use. FDA has no legal authority to interpret patent claims or to adjudicate patent disputes. To the contrary, as FDA acknowledges, its role with respect to patent issues that arise in connection with ANDA applications is "ministerial" only. *See* 68 Fed. Reg. at 36683 (2003).

B. Approval of Hospira's Precedex and the "Orange Book"

15. Hospira is the NDA holder for dexmedetomidine hydrochloride, which it markets under its trademarked brand name, Precedex, pursuant to the FDA's approval of NDA No. 21-038 on December 17, 1999.

16. Hospira is the co-owner and exclusive licensee of U.S. Patent No. 6,716,867 ("the '867 patent"), a method-of-use patent containing two independent claims directed to methods of sedating patients with Precedex in an intensive care unit ("ICU").

17. The publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book") identifies drug products which FDA has approved on the basis of safety and effectiveness under the FDCA. NDA holders may list patents in the Orange Book that cover drug substance (active ingredient), drug product (formulation and composition), and method(s) of use. 21 C.F.R. § 314.53(b)(1). With regard to method of use patents, NDA applicants must also submit for publication in the Orange Book a use code. 21 C.F.R. § 314.53(C)(2)(ii)(P). FDA, in accordance with its purely "ministerial" role, simply lists the NDA holder's use code in the Orange Book. *See* 68 Fed. Reg. at 36,683; 21 C.F.R. § 314.53(f).

18. The FDCA requires that an ANDA filer make one of four certifications with respect to each patent listed in the Orange Book: (i) patent information has not been submitted; (ii) the patent has expired; (iii) the ANDA applicant will not seek final approval before the date the patent expires; and (iv) the patent is invalid, unenforceable, or will not be infringed by the ANDA applicant's product. 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). The last of these is commonly called a paragraph IV certification.

19. The FDCA and FDA regulations provide clear mechanisms for timely and expeditious judicial review and resolution of any patent disputes if an ANDA includes a paragraph IV certification. To ensure that a person who holds an Orange Book-listed patent on an innovator drug has an adequate opportunity to enforce its patent claims before an ANDA application is approved, an ANDA applicant submitting a paragraph IV certification must give

notice to the holder of the patent, which then has a 45-day period in which to bring an action for patent infringement. An action brought within the 45-day period triggers an automatic stay of final FDA approval of the ANDA application until the court rules that the patent is not infringed, or until 30 months have passed, whichever occurs first. These certification and notice requirements enable a patent holder to protect its patent rights without worrying about the irreparable damage (*e.g.*, harm to reputation and irretrievable loss of market share) caused by the immediate flood of generic products to market.

C. FDA's Limited Section viii Authority

20. An ANDA applicant can avoid the paragraph IV process in limited circumstances by seeking approval for unpatented uses of a brand drug. An ANDA applicant seeking approval for unpatented uses of a brand drug must state in its application that it is not seeking approval for an indication covered by a patented method of use, but, instead, is seeking approval only for an approved indication that is not covered by any unexpired patent. This is commonly referred to as a "section viii statement." 21 U.S.C. § 355(j)(2)(A)(viii). An ANDA application that relies on a section viii statement is permissible *only* when (a) FDA has approved more than one indication for the particular drug, *and* (b) at least one of those indications is not covered by any of the brand's patents. *See id.*; 21 C.F.R. § 314.94(a)(12)(iii)(A); *Caraco*, 132 S. Ct. at 1677.

21. While generic drugs must bear the "same" labeling as the brand drug (s*ee, e.g.*, 21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R. § 314.92(a)(1)), in the limited section viii situation described above, generic applicants can propose labeling for the generic drug that redacts, or "carves-out" from the brand drug's approved labeling the patented method(s) of use. *See* 21 C.F.R. § 314.94(a)(8)(iv). However, a carve-out to support a section viii statement can only be

accomplished by, as applicable here, the "omission[s] of an indication or other aspect of labeling protected by [a] patent." 21 C.F.R. § 314.94(a)(8)(iv).

22. As required by law, FDA's clear policy and practice for years has been that it would not approve an ANDA application that relies on a section viii statement if the proposed carved-out indications for use overlap *in any way* with the brand's use code. 68 Fed. Reg. at 36682-83. As FDA stated in 2003, "We have implemented the section viii provisions of the [FDCA] by deferring to the NDA holder's or patent holder's assertion that the method-of-use patent claims an approved use of the drug product." *Id.* at 36682. This approach, FDA observed, allows the NDA applicant holder "to determine which patents claim its approved drug product and then, when appropriate, to resolve disputes over infringement of those patents through patent litigation." *Id.* Without such an approach, FDA continued, ANDA applicants "could always avoid the possibility of a 30-month stay by asserting in a section viii statement that certain labeling for which the applicant is seeking approval is not protected by a listed method-of-use patent—despite the NDA holder's assertion to the contrary—[and] there would be little reason for any applicant to submit a paragraph IV certification for a method-of-use patent." *Id.*

23. Citing and relying upon FDA's above quoted Federal Register statements, the United States Supreme Court recently observed that "*whether section viii is available to a generic manufacturer depends on how the brand describes its patent. Only if the [innovator's] use code provides sufficient space for the generic's proposed label will the FDA approve an ANDA with a section viii statement*." *Caraco*, 132 S. Ct. at 1677 (emphasis added).

24. Thus, if the NDA holder's use code and related narrative for its method-of-use patent overlaps "at all" with any approved indications, the FDA must reject a section viii

statement. *See id.* ("[T]he FDA will not approve such an ANDA if the generic's proposed carve-out label *overlaps at all* with the brand's use code." (emphasis added)). In the event of such an overlap, the section viii route is closed to the ANDA applicant and, if it wishes to proceed, it must do so according to the paragraph IV certification process, with the requisite patent notice to the NDA holder. That is the case here; generic companies cannot make a section viii certification to the FDA because they cannot say that the procedural indication is not encompassed by the '867 patent.

D. FDA's Final Decision of August 18, 2014

25. On August 18, 2014, FDA issued a final decision on Docket No. FDA-2014-N-0087 (Ex. A). FDA decided that "the agency can approve an ANDA that submits a 'section viii' statement and omits labeling that discloses the protected use (as identified by Hospira.)" Ex. A at 1. FDA's Decision is the predicate to FDA's imminent final approval of one or more generic versions of Precedex based upon a section viii statement. Indeed, FDA has approved at least one generic version already, that of Par Sterile Products. But for the August 18 Decision, no section viii approvals would or could be granted. However, FDA's August 18 Decision is impermissible and directly contrary to its established practice, the statute and its regulations, and the decision of the Supreme Court in *Caraco* precisely because the Decision purports to allow FDA to approve an ANDA where there is, as FDA acknowledges in the Decision (Ex. A at 12), overlap with the brand's (Hospira's) use code.

26. The approved indications for Precedex are (a) "sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting, [administered] by continuous infusion not to exceed 24 hours," and (b) "sedation of non-intubated patients prior to and/or during surgical and other procedures." FDA is not authorized to allow an ANDA

applicant for Precedex to rely on a section viii statement to circumvent the paragraph IV certification and notice obligations where, as here, the proposed generic's label overlaps with Hospira's use code. Seven ANDA applicants, all sophisticated pharmaceutical companies, recognized this overlap and instead of filing section viii statements followed the proper and standard procedure and provided the required certifications and notice to Hospira.

27. Some number of ANDA applicants, however, did not make a paragraph IV certification and, instead, sought to rely on a section viii statement. To avoid the possibility that either FDA or an ANDA applicant might fail to see the overlap between Hospira's original use code, "intensive care unit sedation," on the one hand, and the second indication on the label, "sedation of non-intubated patients prior to and/or during surgical and other procedures," on the other, Hospira submitted a clarifying amendment to its original use code narrative on January 6, 2014. Post-January 6, 2014, the use code read as follows: "intensive care unit sedation, including sedation of non-intubated patients prior to and/or during surgical and other procedures." FDA updated the Orange Book on January 8, 2014, to reflect the clarified use code.

28. Hospira's '867 patent use code description plainly overlaps with both of the labeled indications: (a) for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting, and (b) for sedation of non-intubated patients prior to and/or during surgical and other procedures where those procedures take place in an intensive care unit ("ICU").

29. That this second indication is used in practice to treat patients in an ICU is well established. Doctors routinely use Precedex to sedate *non*-intubated patients in the ICU. As Dr. Bruce Friedman, the Co-Director and Critical Care Director of the largest burn center in the

United States, stated in a declaration submitted with Hospira's comments on the FDA docket, he very frequently uses Precedex for the sedation of non-intubated patients prior to and/or during surgical and other procedures on patients in the ICU. Ex. B. Studies confirm his first-hand testimony. One case report, for example, demonstrates the successful use of dexmedetomidine to sedate an ICU patient for awake fiberoptic intubation, a procedure specifically referenced in the labeling for the second indication. *See* Maxime Madhere et al., *Dexmedetomidine as Sole Agent for Awake Fiberoptic Intubation in a Patient with Local Anesthetic Allergy*, 25 J. Anesthesia 592-94 (2011).

E. FDA's Unorthodox and Unlawful "Rulemaking Lite" Approach

30. Hospira wrote to the FDA's Chief Counsel, also on January 6, 2014, requesting that FDA confirm that it would not grant final approval to any ANDA for generic Precedex based on a section viii statement. Hospira explained that the '867 patent and the use code before and after clarification overlap with both of the approved indications for Precedex, that this is unequivocally clear from a comparison of the use code and approved indications, and, accordingly, FDA should and was required to deny any ANDA application that purported to rely on a section viii statement.

31. FDA declined to confirm that it would deny final approval to any ANDA for a generic version of Precedex that was based on a section viii statement. Instead, on January 15, 2014, FDA sent a letter to Hospira, as the NDA holder, and "to all applicants who submitted Abbreviated New Drug Applications (ANDAs) to the [FDA] referencing Precedex," soliciting comments on a public online docket, Docket No. FDA-2014-N-0087. Ex. C ("Dear Applicant Letter").

32. FDA's Dear Applicant Letter was an extraordinary agency action for a number of reasons: *First*, in the letter FDA clearly acknowledged the overlap between the Hospira use code and Precedex's approved indications but, nevertheless, sought comments from ANDA applicants about the legality of a section viii carve-out notwithstanding the overlap. *Second*, the letter made the novel suggestion that the overlap between Hospira's use code and Precedex's approved indications for use could be circumvented by allowing an ANDA applicant to *add* words to, rather than *omit* words from the approved indications, a suggestion contrary to an FDA regulation which provides that a proper carve-out can be accomplished only by the "*omission* of an indication or other aspect of labeling protected by patent." *See* 21 C.F.R. § 314.92(a)(1), (a)(8)(iv) (emphasis added). *Third*, the letter was sent to only a very small subset of persons—"Dear Dexmedetomidine Hydrochloride Injection NDA/ANDA Applicant"—and not the larger population of parties that would be affected by FDA rulemaking on these points. *Fourth*, commenters were given a very short period of time to respond – initial comments were due within 9 days and comments in response to initial comments were due a mere 7 days later.

33. In response to the Dear Applicant Letter, FDA received multiple comments. As one of the commenters noted, "[t]he issues raised by the FDA have created a firestorm of controversy, and a tangled web of conflicting legal interpretations," which it illustrated with a matrix documenting the utter lack of any consensus among the commenters. Some commenters advocated that the FDA should apply its own policies and rules and deny ANDAs based on section viii carve-outs. Other commenters argued that section viii statements were a permissible pathway to approval, but even among this group there was no agreement on the "correct" approach. Some advocated adding language to the indications for use on the approved labeling, recognizing the impossibility of avoiding the overlap between Hospira's use code and the

indications in their approved form. Others advocated FDA's suggestion that a use code could be ignored if the FDA decided, by some indeterminate methodology, that it was offered too late. Some suggested that either method of circumventing the use code would be appropriate. The comments are available online at http://www.regulations.gov/#!docketDetail;D=FDA-2014-N-0087.

34. Hospira submitted comments stating that, under existing law and practice, an ANDA that relied on a section viii statement should be denied because Precedex's indications for use and Hospira's use code statements overlapped. Hospira further contended that if the FDA adopted any of the methods for circumventing Hospira's use code that it had proposed in the Dear Applicant Letter, it would be deviating from its own established policies and rules and engaging in unlawful rulemaking in the context of reviewing an ANDA.

35. Two other commenters whose memberships include strong representation from the bio-pharmaceutical sector, Biotechnology Industry Organization and Illinois Biotechnology Industry Organization ("iBIO"), objected to the "limited" and "narrow" request for commentary, as well as the abbreviated docket process in lieu of following the notice and comment procedures required by the APA.

36. On August 18, 2014, FDA issued its Decision on the docket. Ex. A. This Decision authorizes imminent approval to one or more pending ANDAs for approval to market a generic version of Precedex based on improper section viii statements. FDA granted at least one such approval on the same day as its Decision.

F. FDA's Action Irreparably Harms Hospira

37. FDA's Decision threatens to cause and will cause imminent irreparable harm to Hospira. The irreparable harm to Hospira is detailed in the Declaration of Mr. Thomas Moore

filed in support of Hospira's accompanying motion for temporary and preliminary injunctive relief. The Moore Declaration is hereby adopted and incorporated by reference.

38. Hospira expects that the consequence of FDA's final approval of an ANDA for a generic version of Precedex that the generic supplier(s) will be that the market is flooded with generic product, placing at least six months' worth of generic product into the wholesale distribution channel within days of final approval, in a concerted effort to secure the most favorable position vis-à-vis other generic entrants.

39. Product wholesalers and hospital providers have been contacted by at least two prospective companies regarding a generic version of Precedex. One of those companies, in December 2013, entered into a contract with a large group purchasing organization (Novation) to provide generic Precedex, and offered its product at a unit price 45% lower than that of the current Precedex brand price. That company was promising to launch on "day one" following FDA approval. In August 2014, another large group purchasing organization was approached by another of those companies offering a 25% discount to the current Precedex brand price with an expected approval and launch date of September 1, 2014.

40. A consequence of generic launch at the proposed sharply reduced price will be that Hospira will almost immediately be forced to terminate its entire U.S. brand drug sales force of approximately 130 persons. With generic competition, customers will purchase product through drug wholesalers at the lowest available price and regardless of brand. As such, Hospira will have neither reason nor need to continue to have a sales force to visit prescribers and hospital providers. The loss of the sales force will further harm Hospira by eliminating the expected growth in the sales of Precedex. That growth is directly dependent on the education efforts of the sales force. Hospira will also likely be caused to reduce additional corporate staff

as a result of premature generic entry. If injunctive relief is denied and Hospira ultimately prevails on the merits, Hospira will be unable to rehire its lost sales force because they will have moved on to other jobs.

41. Precedex sales and market share will immediately and significantly erode upon entry of a generic version of Precedex to market. Both of these harms will be irreparable. One generic is proposing to sell its product at a 45% reduction on Hospira's unit price; once a number of generics are on the market, this price reduction will become even steeper. Hospira would have to significantly drop its price to compete with the generic competitors' drug. Even if Hospira were successful and ultimately able to prevent generics from further sales beyond what occurs in the first days after approval, the market would not return to pre-generic prices as customers typically enter into two- to three-year contracts to purchase drugs.

42. Considering the expected Sandoz generic launch in December 2014, a premature generic launch will effectively eliminate Hospira's remaining period as the exclusive supplier of Precedex as multiple months of generic product will be placed into the wholesale distribution channel. With a premature generic entry, Hospira would lose tens of millions of dollars, if not more than a hundred million dollars, in profits even if it is successful in preventing further generic sales beyond what occurs in the first days after approval, and is ultimately successful in this matter. Hospira's loss of revenue and profit as a result of a premature generic entry, while a financial or monetary loss, is itself irreparable because the loss can neither be quantified nor will Hospira be compensated for this loss, even if Hospira ultimately prevails in this action. Furthermore, Hospira will have no means to recover its losses because FDA's sovereign immunity would preclude Hospira from recovering money damages.

43. Losing these profits will hinder Hospira's ability to fund research and development on new drug products that Hospira would like to bring to market in the future. Revenue from Precedex has allowed Hospira to commit enormous resources toward the research and development of multiple generic and biosimilar drug programs, products which are crucial to FDA's mission of providing safe, effective, and affordable drugs to the public at large. Reduced funding of those programs due to a premature generic entry for Precedex will likely delay or eliminate some of those programs.

44. Hospira will be forced to stop funding clinical trials for Precedex, to the extent possible, in the event of a premature generic entry. The public would face a significant loss as a result; Hospira has conducted or supported extremely important, breakthrough clinical trials that have greatly impacted the healthcare and patient communities. The growth of Precedex – and its potential new uses – will be curtailed as a result of premature generic entry.

45. Accordingly, Hospira seeks and is entitled to temporary and preliminary injunctive relief pending the determination of this case on the merits.

Count One – Violation of 21 U.S.C. § 355(j)(2)(A)(viii)

46. Hospira incorporates by reference the allegations contained in Paragraphs 1 through 45 of this complaint.

47. FDA's August 18 Decision in Docket No. FDA-2014-N-0087 authorizes imminent approval of a generic version of Precedex based on a section viii statement and at least one such approval has occurred. FDA's Decision and the ANDA approval actions which flow form it are contrary to law and arbitrary and capricious because the generic's proposed label overlaps with Hospira's use code. FDA's action or decision is unlawful. *See* 21 U.S.C. § 355(j)(2)(A)(viii).

48. As the Supreme Court noted in *Caraco*, "the FDA will not approve such an ANDA if the generic's proposed carve-out label *overlaps at all* with the brand's use code." 132 S. Ct. at 1677 (emphasis added). The Court's observation is based upon FDA's being prohibited from "approv[ing] such an ANDA" by 21 U.S.C. § 355(j)(2)(A)(viii). Here, notwithstanding that statutory prohibition, FDA's Decision has resulted in a wrongful and unlawful approval of "an ANDA [where] the generic's carve-out label overlaps . . . with [Hospira's] use code." Indeed, FDA's Decision expressly acknowledges that ANDAs for Precedex may "be approved for procedural sedation despite the fact that use for procedural sedation may at times occur in an intensive care setting." Ex. A at 12. FDA's August 18 Decision and any ANDA approvals flowing from that Decision are thus contrary to law. *See* 5 U.S.C. § 706(2)(a).

49. In accordance with law, FDA's clear policy and practice for years has been that it would not approve an ANDA application that relies on a section viii statement if the proposed carved-out indications for use overlap *in any way* with the brand's use code. 68 Fed. Reg. at 36682-83. As FDA stated in 2003, "We have implemented the section viii provisions of the [FDCA] by deferring to the NDA holder's or patent holder's assertion that the method-of-use patent claims an approved use of the drug product." *Id.* at 36682. This approach, FDA observed, allows the NDA applicant holder "to determine which patents claim its approved drug product and then, when appropriate, to resolve disputes over infringement of those patents through patent litigation." *Id.* Without such an approach, FDA continued, ANDA applicants "could always avoid the possibility of a 30-month stay by asserting in a section viii statement that certain labeling for which the applicant is seeking approval is not protected by a listed method-of-use patent—despite the NDA holder's assertion to the contrary—[and] there would be little reason for any applicant to submit a paragraph IV certification for a method-of-use patent."

Id. In contrast to 2003 when FDA understood and followed the law, FDA's August 18 Decision is contrary to law and is arbitrary and capricious. The August 18 Decision allows ANDA applicants to "avoid the possibility of a 30-month stay by asserting in a section viii statement that certain labeling for which the applicant is seeking approval is not protected by a listed method-of-use patent—despite the NDA holder's assertion to the contrary." Under this approach, "there would be little reason for any applicant to submit a paragraph IV certification for a method-of-use patent."

Count Two – Violation of APA Rulemaking Requirements

50. Hospira incorporates by reference the allegations contained in Paragraphs 1 through 49 of this complaint.

51. The FDA is an agency subject to the requirements of the APA. 5 U.S.C. § 701(b)(1). This includes the APA's requirements for rulemaking. FDA is prohibited from applying a "rule," as defined in the APA, if that rule has not been adopted properly in accordance with the APA. *See id.* §§ 553(b)-(d), 706(2)(a). The rule announced in FDA's August 18 Decision is a "rule" within the meaning of the APA, which rule was not adopted in accordance with the rulemaking requirements of the APA.

52. An ANDA application that relies on a section viii statement is permissible *only* when (a) FDA has approved more than one indication for the particular drug, *and* (b) at least one of those indications is not covered by any of the brand's patents. *See id.*; 21 C.F.R. § 314.94(a)(12)(iii)(A); *Caraco*, 132 S. Ct. 1677. In that limited situation, generic applicants may propose labeling for the generic drug that redacts, or "carves-out" from the brand drug's approved labeling the patented methods of use. *See* 21 C.F.R. § 314.94(a)(8)(iv). FDA may approve a modified "carve-out" label in this instance. *See* 21 C.F.R. § 314.127(a)(7). But, a

carve-out to support a section viii statement may only be accomplished by the "omission[s] of an indication or other aspect of labeling protected by [a] patent." 21 C.F.R. § 314.94(a)(8)(iv).

53. FDA's new rule is directly contrary to what is authorized by Supreme Court precedent, statute, and existing regulations. Assuming, without conceding, that FDA could lawfully adopt a properly promulgated regulation to do that which it has done here (to allow approval of an ANDA where there is conceded overlap between a patent protected use and as approved ANDA's use), FDA plainly cannot adopt such a new rule by the unauthorized, unorthodox, and unlawful approach it followed here. If FDA is to change settled law, *see Caraco*, as it has here by adopting a new rule, it must do so lawfully pursuant the rulemaking requirements and procedures of the APA. FDA failed to do so here.

54. FDA's decision which allows approval of an ANDA in the face of clear overlap between the generic's proposed label and Hospira's use code is a new and unlawfully adopted rule or regulation.

55. The APA requires an agency engaged in rulemaking to: (1) provide adequate advance notice and publication of the proposed rule in the *Federal Register*, 5 U.S.C. § 553(b); (2) afford all interested persons (including members of the public) an opportunity to participate through the submission of written data, views, or arguments, *id.* (c); and (3) publish the final rule in the *Federal Register* with a statement of basis and purpose not less than thirty days before its effective date, *id.* (c), (d).

56. FDA's process here fell very far short of what the APA requires. FDA failed to provide adequate notice and publication of the proposed rule in the *Federal Register*; only requested comments from an agency-selected and limited pool of commenters (as distinguished from all "interested persons"); provided only a short period in which to comment (as

distinguished from adequate advance notice and publication in the *Federal Register*); and FDA failed to publish in the Federal Register a final rule that adequately discussed the many divergent comments.

57. Because FDA did not comply with the rulemaking requirements of the APA, the rule applied in this matter is invalid and any generic product approval decision based upon that rule is equally and necessarily invalid. *See* 5 U.S.C. § 706(2)(a)

Prayers for Relief

WHEREFORE, Hospira prays as follows:

(a) that pending the determination of this matter on the merits, the Court grant Hospira's motion for temporary and/or preliminary injunctive relief and order FDA to rescind ab initio any final ANDA approval of a generic version of Precedex based upon the August 18 Decision in Docket No. FDA-2014-N-0087, order FDA to recall any product sold or distributed under such an approval, and enjoin FDA from granting any further or additional final ANDA approval actions based upon the August 18 Decision in Docket No. FDA-2014-N-0087;

(b) that the Court grant such other temporary, preliminary, or interim relief as may be necessary to protect Hospira's rights pending the determination of this case on the merits;

(c) that the Court declare that FDA's August 18 Decision in Docket No. FDA-2014-N-0087 which authorizes imminent approval of generic versions of Precedex based upon a section viii statement is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;

(d) that the Court declare that FDA's August 18 Decision in Docket No. FDA-2014-N-0087 is a "rule" or "regulation" within the meaning of the APA which is invalid because it

was not lawfully adopted, and further declare that any FDA action approving generic versions of Precedex based upon a section viii statement is unlawful;

(e) that the preliminary injunctions be made permanent; and

(f) that the Court grant such other, further, and additional relief as the nature of the cause may require.

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